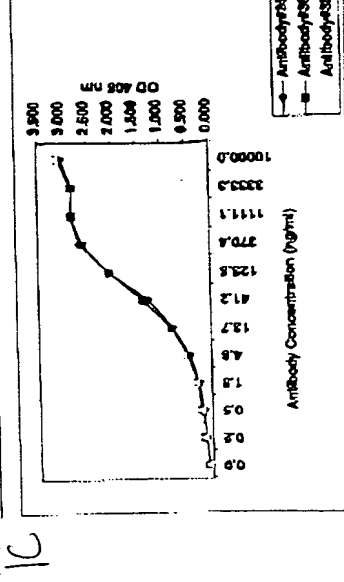
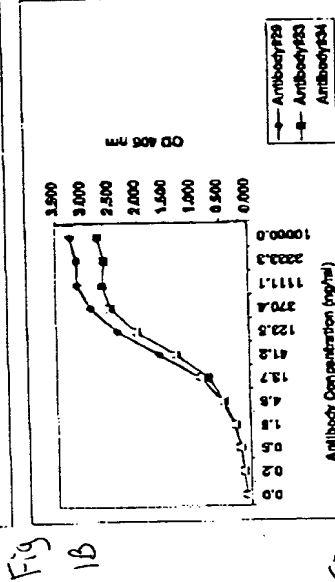
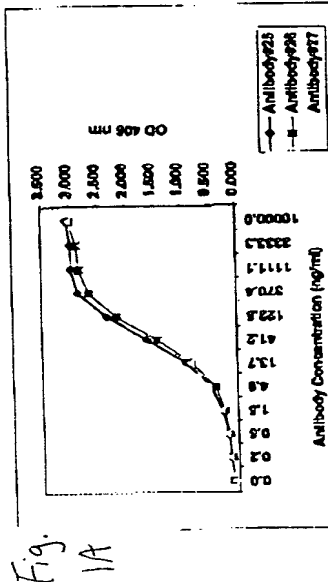
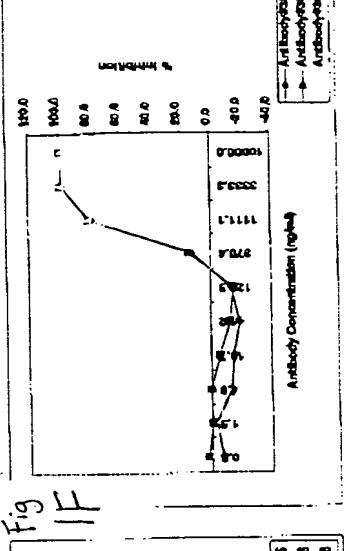
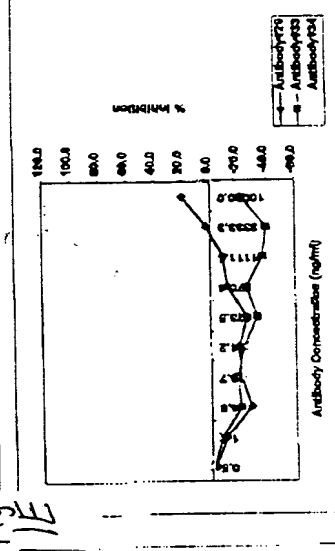
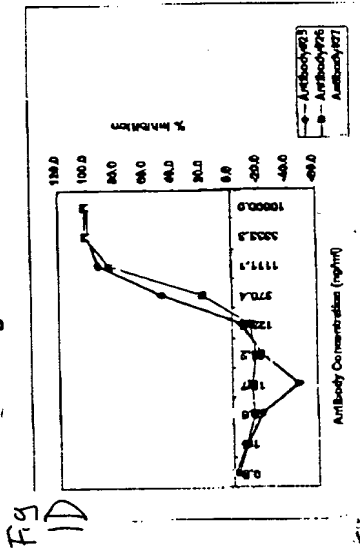


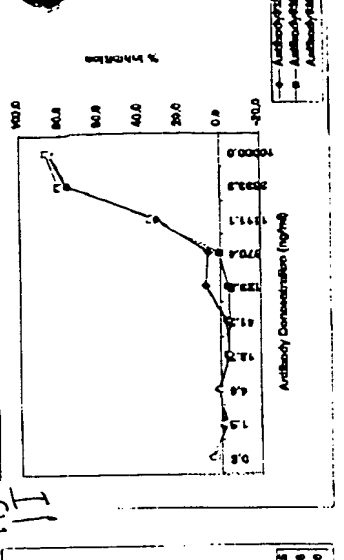
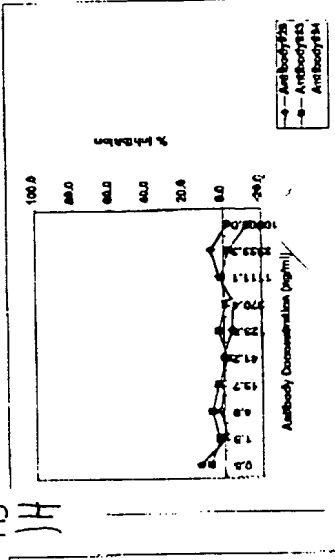
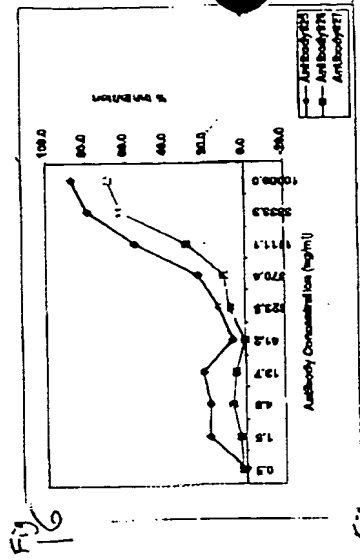
Binding of antibodies to CTLA-4



Blockage of CD86 binding



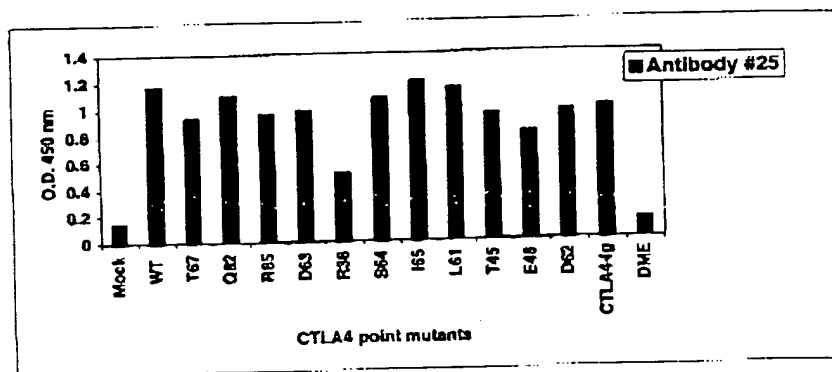
Blockage of CD80 binding



Anti-CTLA4 Abs #25, #26, and #29 defined three distinct epitopes on CTLA4

Fig.
2A

CTLA4 point mutant	Antibody #25
Mock	0.165
WT	1.17
T67	0.935
Q82	1.1
R85	0.96
D63	0.988
R38	0.52
S84	1.07
I65	1.19
L61	1.14
T45	0.948
E48	0.811
D62	0.985
CTLA4-Ig	0.996
DME	0.14



CTLA4 point mutant	Antibody #26
Mock	0.174
WT	1.16
T67	0.944
Q82	1.07
R85	0.976
D63	0.979
R38	0.636
S84	1.1
I65	1.17
L61	1.19
T45	0.948
E48	0.18
D62	0.974
CTLA4-Ig	1.1
DME	0.183

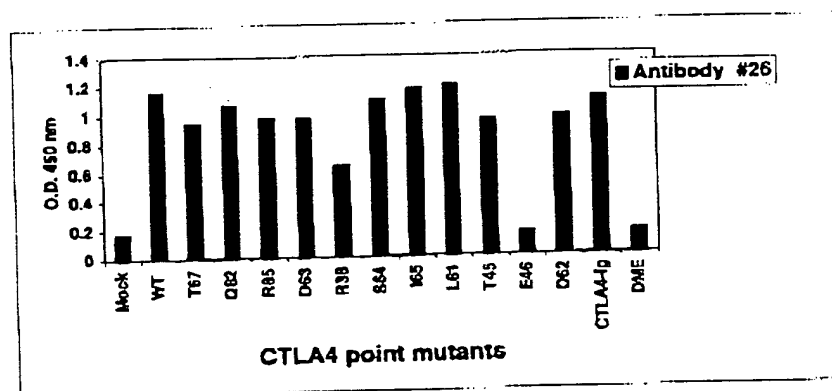


Fig.
2B

CTLA4 point mutant	Antibody #29
Mock	0.094
WT	0.82
T67	0.695
Q82	0.784
R85	0.096
D63	0.719
R38	0.364
S84	0.753
I65	0.801
L61	0.819
T45	0.885
E48	0.609
D62	0.673
CTLA4-Ig	0.857
DME	0.091

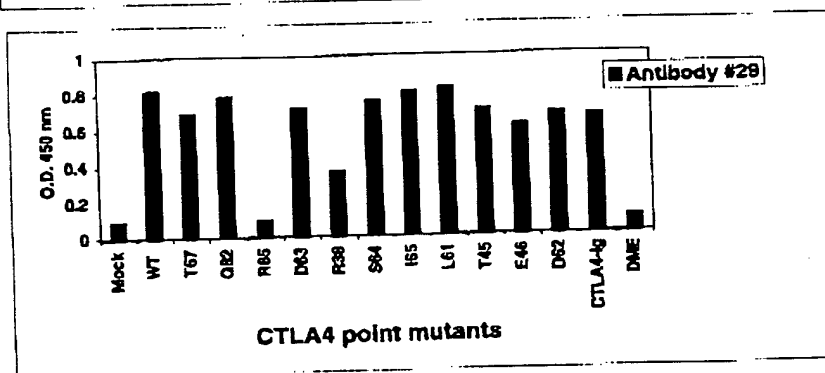


Fig.
2C

Fig 3A Proliferation

	media	Ab #25	Ab #26	Ab#27	Ab#29	Ab#33	Ab#34	Ab#35	Ab#36	Ab #38
Donor 1	54871	16589	33928	49492	234	928	45524	56203	72358	50665
Donor 2	102159	32784.3	58736.2	78098.2	1891.3	5427.4	78391.9	91920.2	116454.6	88937.9

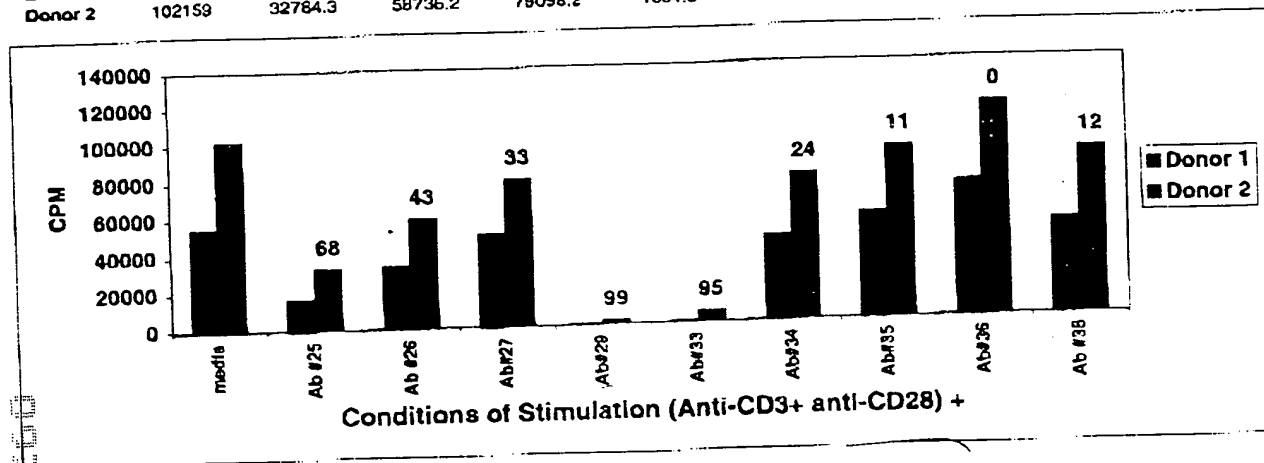


Fig 3B IL-2 Production

	media	Ab #25	Ab #26	Ab#27	Ab#29	Ab#33	Ab#34	Ab#35	Ab#36	Ab #38
IL-2(pg/ml)	2125.3	330.2	182.5	231.7	60.8	462.3	573.7	305.7	617.7	672.1

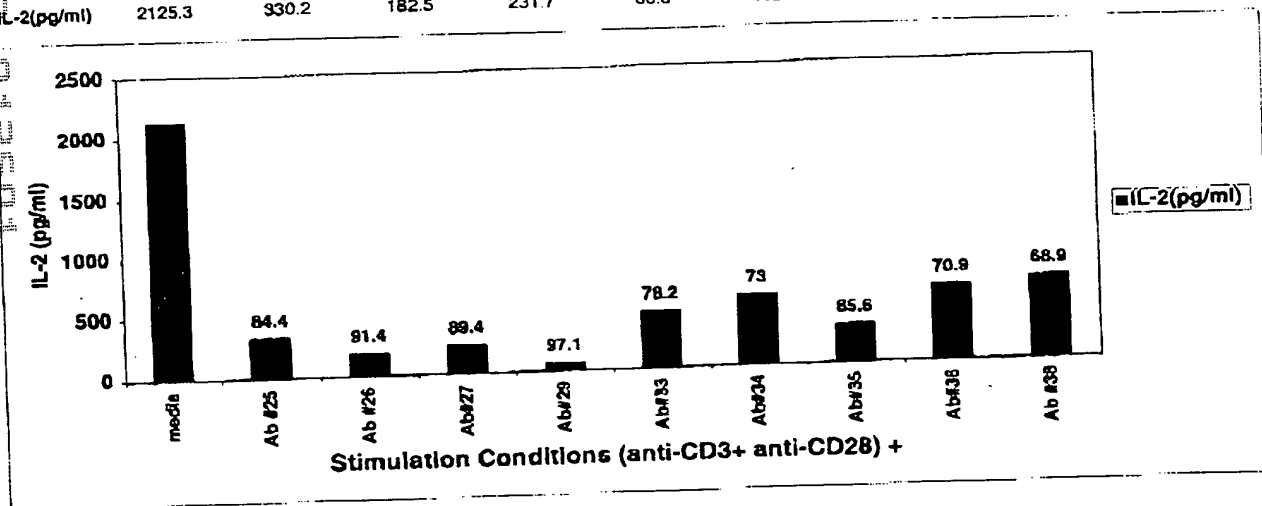


Fig. 4A Proliferation

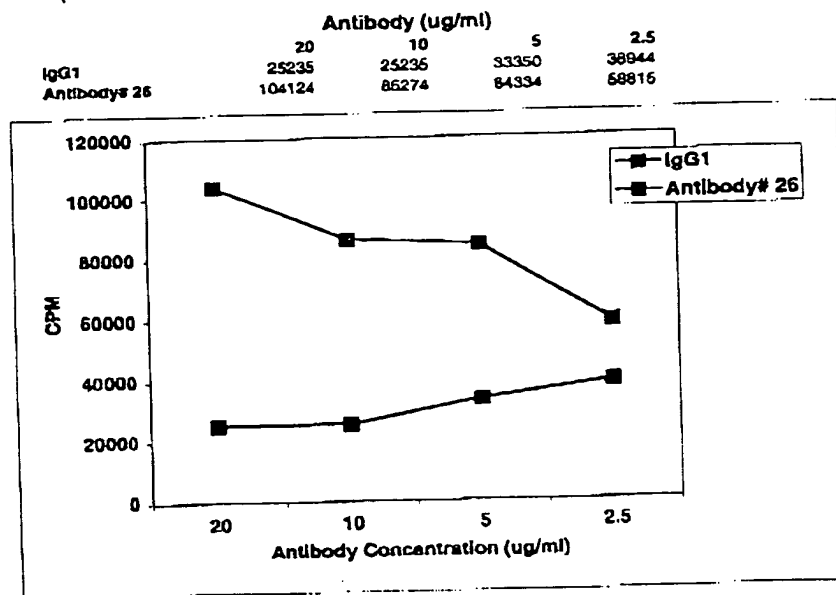
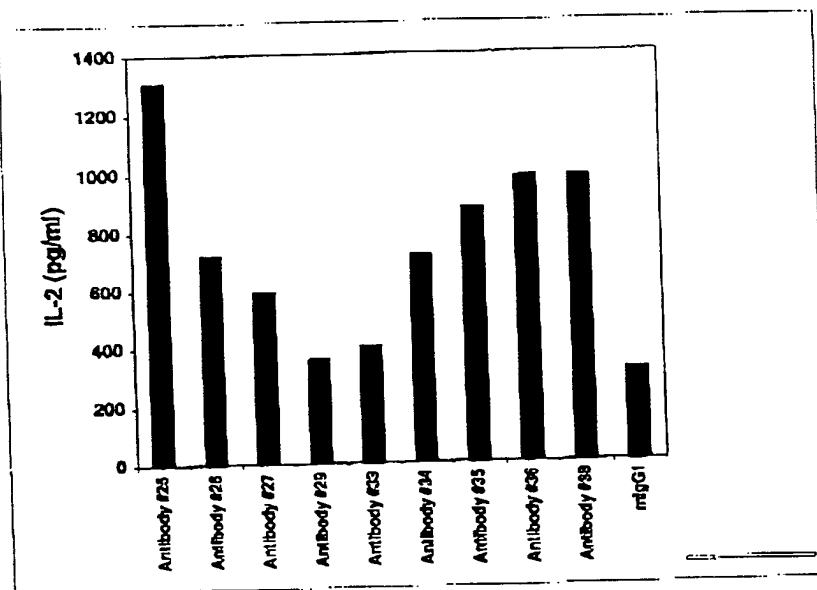


Fig 4B IL-2 Production

Antibody	IL-2 (pg/ml)
Antibody #25	1310
Antibody #26	720
Antibody #27	584
Antibody #29	358
Antibody #33	400
Antibody #34	715
Antibody #35	875
Antibody #36	982
Antibody #38	982
mIgG1	317



FOUO-FOUO-FOUO

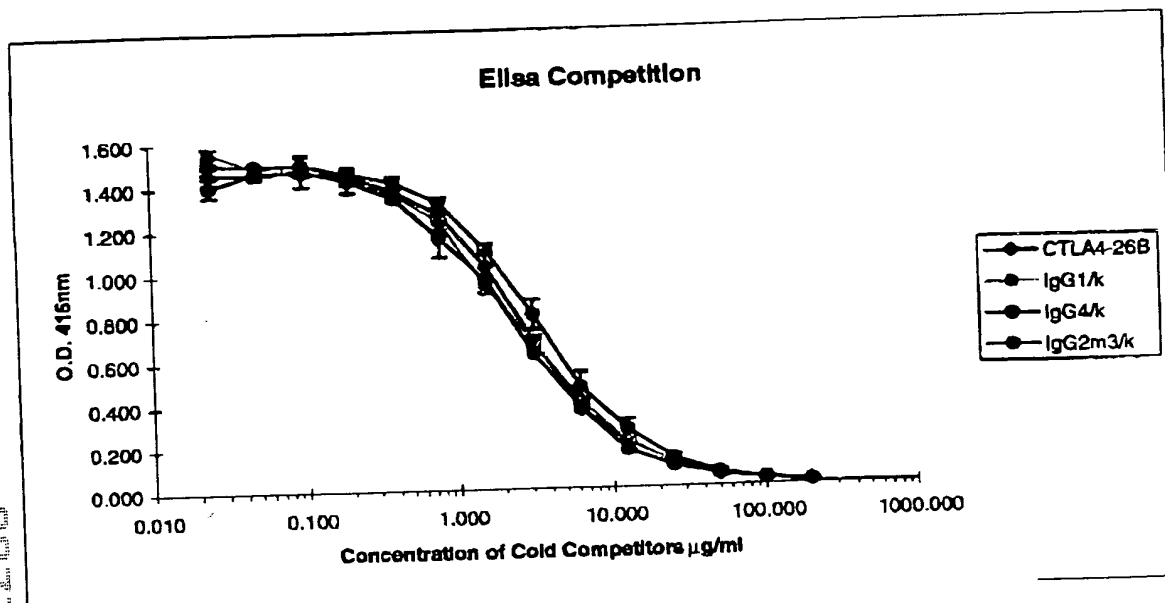
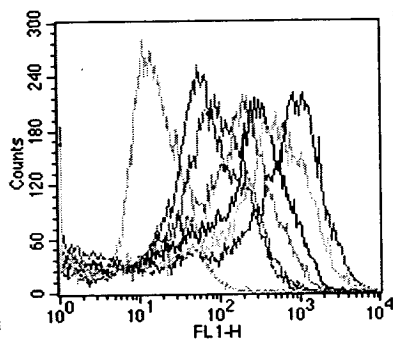


Figure 5

FACS Competition Using FITC-Labeled CTLA4-26B with Cold CTLA4-26B and Humanized IgG1/κ

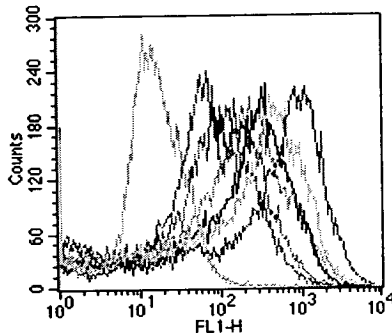
Name	Cell Line	Primary Ab	Competitor
052199.001	CHO.CTLA4	FITC-CTLA4-26B 125 ng	2000 ng
052199.002			1000 ng
052199.003			500 ng
052199.004			250 ng
052199.005			100 ng
052199.006	CHO.B7.1	none	IgG1/κ
052199.007			2000 ng
052199.008			1000 ng
052199.009			500 ng
052199.010			250 ng
052199.016			100 ng
052199.017			none
052199.018			125 ng
052199.019			none
			none

Fig. 6A



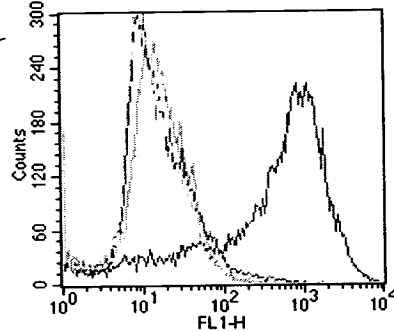
Key	Name	Parameter	Gate
---	052199.016	FL1-H	No Gate
---	052199.017	FL1-H	No Gate
---	052199.001	FL1-H	No Gate
---	052199.002	FL1-H	No Gate
---	052199.003	FL1-H	No Gate
---	052199.004	FL1-H	No Gate
---	052199.005	FL1-H	No Gate

Fig. 6B



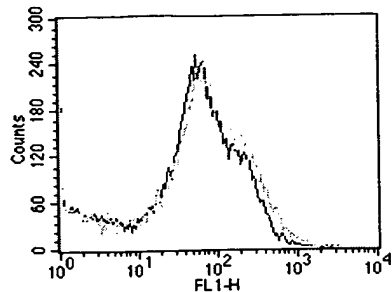
Key	Name	Parameter	Gate
---	052199.016	FL1-H	No Gate
---	052199.017	FL1-H	No Gate
---	052199.006	FL1-H	No Gate
---	052199.007	FL1-H	No Gate
---	052199.008	FL1-H	No Gate
---	052199.009	FL1-H	No Gate
---	052199.010	FL1-H	No Gate

Fig. 6C



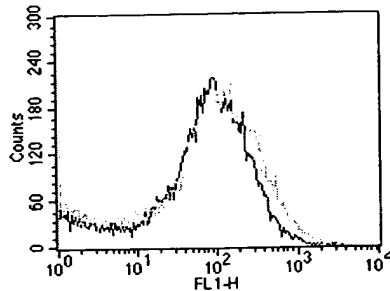
Key	Name	Parameter	Gate
---	052199.016	FL1-H	No Gate
---	052199.017	FL1-H	No Gate
---	052199.018	FL1-H	No Gate
---	052199.019	FL1-H	No Gate

Fig.
7A



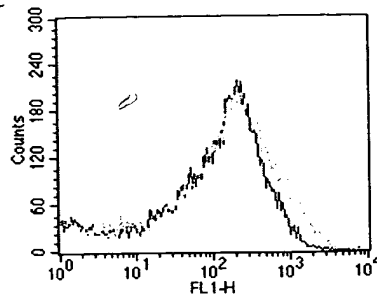
Key	Name	Parameter	Gate
—	052199.001	FL1-H	No Gate
—	052199.006	FL1-H	No Gate

Fig
7B



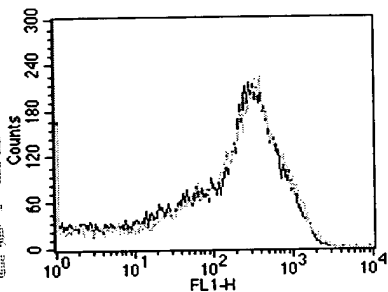
Key	Name	Parameter	Gate
—	052199.002	FL1-H	No Gate
—	052199.007	FL1-H	No Gate

Fig
7C



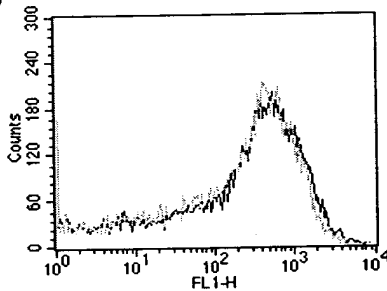
Key	Name	Parameter	Gate
—	052199.003	FL1-H	No Gate
—	052199.008	FL1-H	No Gate

Fig
7D



Key	Name	Parameter	Gate
—	052199.004	FL1-H	No Gate
—	052199.009	FL1-H	No Gate

Fig
7E



Key	Name	Parameter	Gate
—	052199.005	FL1-H	No Gate
—	052199.010	FL1-H	No Gate

Figure 7

Fig 8A

Jurkat CTLA4 NEGATIVE cell line

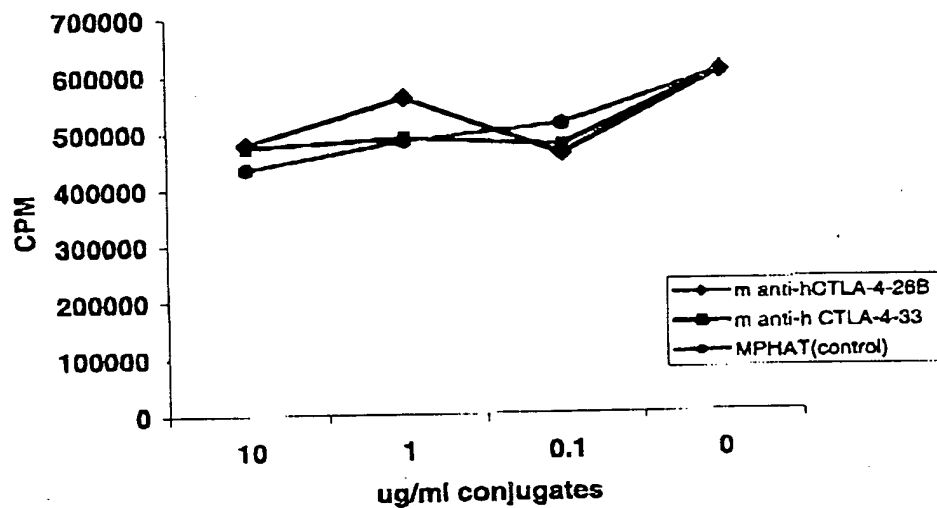
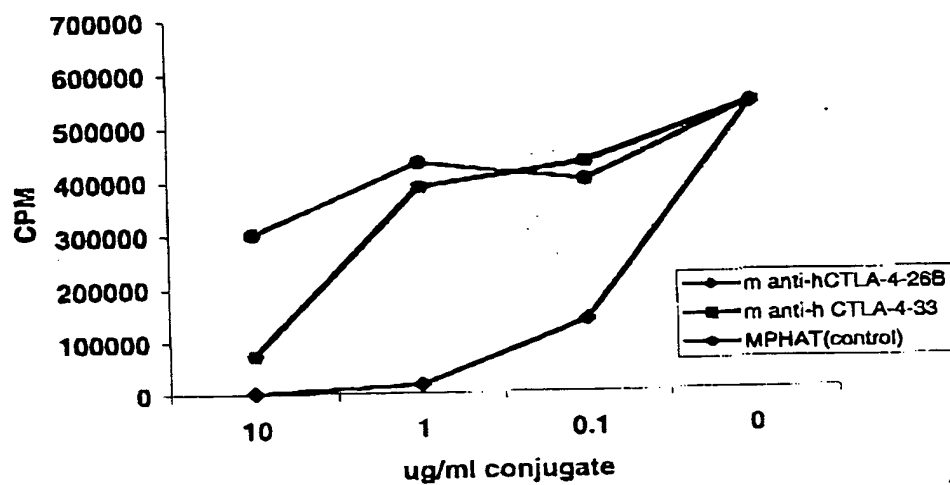


Fig 8B

Jurkat CTLA-4 POSITIVE cell line



HuCTLA4 - Vk

TATATCTAGACCACCATGGATTTTCAAGTGCAGATCTTCAGCTTCCTGCTAATCAGTGCC
M D F Q V Q I F S F L L I S A

TCAGTCATACTGTCCAGAGGAGATATCCAGATGACCCAGTCTCCATCCTCCCTATCCGCA
S V I L S R G D I Q M T Q S P S S L S A

TCTGTTGGGGACAGGGTCACCATAACCTGTAGTGCCACCTCAAGTATAACTTACATGTCC
S V G D R V T I T C S A T S S I T Y M S

TGGTATCAGCAGAAGCCAGGAAAGGCTCCCAAGCTTCTGATTTATGACACATCCAACCTG
W Y Q Q K P G K A P K L L I Y D T S N L

GCTTCTGGGGTACCTAGCCGCTTCAGTGGCAGTGGGTCTGGGACCGACTACACACTCACA
A S G V P S R F S G S G S G T D Y T L T

ATCAGCAGCCTGCAGCCAGAAGATTTTGCCACTTATTACTGCCAGCAGTGGAGTAGTTAC
I S S L Q P E D F A T Y Y C Q Q W S S Y

CCGCTCACGTTTCGGTGGAGGGACCAAGGTTGAGATAAAACGTAAGTAGAATCCAAAGTCT
P L T F G G G T K V E I K

AGATATA

Figure 9

007210-01501

HuCTLA4 - VH

TATATCTAGACCACCATGGCTGTCCTGGTGCTGTTCTCTGCCTGGTTGCATTTCCAAGC
M A V L V L F L C L V A F P S

TGTGTCCTGTCCCAGGTGCAGCTGCAAGAGTCAGGACCTGGCCTGGTGAAGCCCTCACAG
C V L S Q V Q L Q E S G P G L V K P S Q

ACACTGTCCTTGACTTGCACTGTCTCTGGGTTTTTCATTAACCTCATATGGTGTATATTGG
T L S L T C T V S G F S L T S Y G V Y W

GTTCCGCCAGCCTCCAGGAAAGGGTCTGGAGTGGCTGGGAGTAATATGGGCTGGTGGTACC
V R Q P P G K G L E W L G V I W A G G T

ACAAATTATAATTCGGCTCTCATGTCCAGACTGACAATCAGCAAAGACACATCCAAGAAC
T N Y N S A L M S R L T I S K D T S K N

CAAGTTTCTTAAACTCAGCAGTGTGACTGCAGCGGACACAGCCGTCTACTACTGTGCC
Q V S L K L S S V T A A D T A V Y Y C A

CGAGGCCCCCGCACGCTATGATGAAGAGAGGCTATGCTATGGACTACTGGGGACAAGGA
R G P P H A M M K R G Y A M D Y W G Q G

ACCCTAGTCACAGTCTCCTCAGGTGAGTCCTTAAACCTCTAGATATA
T L V T V S S

Figure 1D

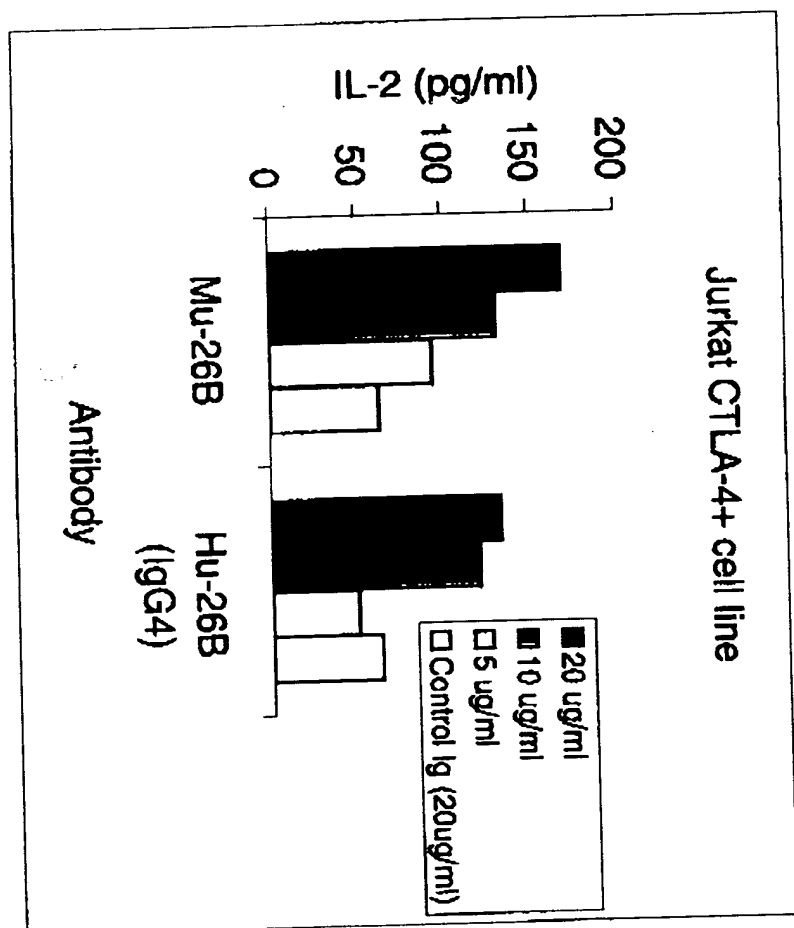


Figure 11

0072403-042504